EXHIBIT O

The United States Pharmacopeia

TWENTY-FIRST REVISION

Official from January 1, 1985

The National Formulary

SIXTEENTH EDITION

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United States Pharmacopeial Convention, Inc.
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standardization of laboratory reference standards, reagents, and standard solutions.

(d) Complete records shall be maintained of the periodic calibration of laboratory instruments, apparatus, gauges, and recording devices required by § 211.160 (b) (4).

(e) Complete records shall be maintained of all stability testing performed in accordance with § 211.166.

§ 211.196 Distribution records.

Distribution records shall contain the name and strength of the product and a description of the dosage form, name and address of the consignee, date and quantity shipped, and lot or control number of the drug product.

§ 211.198 Complaint files.

(a) Written procedures describing the handling of all written and oral complaints regarding a drug product shall be established and followed. Such procedures shall include provisions for review by the quality control unit, of any complaint involving the possible failure of a drug product to meet any of its specifications and, for such drug products, a determination as to the need for an investigation in accordance with § 211.192.

(b) A written record of each complaint shall be maintained in a file designated for drug product complaints. The file regarding such drug product complaints shall be maintained at the establishment where the drug product involved was manufactured, processed, or packed, or such file may be maintained at another facility if the written records in such files are readily available for inspection at that other facility. Written records involving a drug product shall be maintained until at least 1 year after the expiration date of the drug product, or 1 year after the date that the complaint was received, whichever is longer. In the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under § 211.137, such written records shall be maintained for 3 years after distribution of the drug product.

(1) The written record shall include the following information, where known: the name and strength of the drug product, lot number, name of complainant, nature of complaint, and reply to complainant.

(2) Where an investigation under § 211.192 is conducted, the written record shall include the findings of the investigation and followup. The record or copy of the record of the investigation shall be maintained at the establishment where the investigation occurred in accordance with § 211.180 (c).

(3) Where an investigation under § 211.192 is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.

Subpart K—Returned and Salvaged Drug Products

§ 211.204 Returned drug products.

Returned drug products shall be identified as such and held. If the conditions under which returned drug products have been held, stored, or shipped before or during their return, or if the condition of the drug product, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality or purity of the drug product, the returned drug product shall be destroyed unless examination, testing, or other investigations prove the drug product meets appropriate standards of safety, identity, strength, quality, or purity. A drug product may be reprocessed provided the subsequent drug product meets appropriate standards, specifications, and characteristics. Records of returned drug products shall be maintained and shall include the name and label potency of the drug product dosage form, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned drug product. If the reason for a drug product being returned implicates associated batches, an appropriate investigation shall be conducted in accordance with the requirements of § 211.192. Procedures for the holding, testing, and reprocessing of returned drug products shall be in writing and shall be followed.

§ 211.208 Drug product salvaging.

Drug products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether drug products have been subjected to such conditions, salvaging operations may be conducted only if there is (a) evidence from laboratory tests and assays (including animal feeding studies where applicable) that the drug products meet all applicable standards of identity, strength, quality, and purity and (b) evidence from inspection of the premises that the drug products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Organoleptic examinations shall be acceptable only as supplemental evidence that the drug products meet appropriate standards of identity, strength, quality, and purity. Records including name, lot number, and disposition shall be maintained for drug products subject to this section.

⟨1081⟩ GEL STRENGTH OF GELATIN

Pipet 105 mL of water at 10° to 15° into a standard Bloom bottle, add 7.5 g of Gelatin, and stir. Allow to stand for 1 hour, then bring to a temperature of 62° in 15 minutes by placing in a water bath regulated at 65° (the substance may be swirled several times to aid solution). Finally mix by inversion, allow to stand for 15 minutes, and place in a water bath at 10 ± 0.1°. Chill, without disturbance, for 17 hours. Determine the gel strength in a Bloom Gelometer (a device developed to make this determination under standardized conditions) adjusted for 4-mm depression and to deliver 200 ± 5 g of shot per 5 seconds, using the 12.7-mm diameter (nonbeveled) plunger.

⟨1101⟩ MEDICINE DROPPER

The Pharmacopeial medicine dropper consists of a tube made of glass or other suitable transparent material that generally is fitted with a collapsible bulb and, while varying in capacity, is constricted at the delivery end to a round opening having an external diameter of about 3 mm. The dropper, when held vertically, delivers water in drops each of which weighs between 45 mg and 55 mg.

In using a medicine dropper, one should keep in mind that few medicinal liquids have the same surface and flow characteristics as water, and therefore the size of drops varies materially from one preparation to another.

Where accuracy of dosage is important, a dropper that has been calibrated especially for the preparation with which it is supplied should be employed. The volume error incurred in measuring any liquid by means of a calibrated dropper should not exceed 15%, under normal use conditions.

⟨1111⟩ MICROBIOLOGICAL ATTRIBUTES OF NON-STERILE PHARMACEUTICAL PRODUCTS

Few raw materials used in making pharmaceutical products are sterile as received, and special treatment may be required to render them microbiologically acceptable for use. Strict adherence to hygienic practices in pharmaceutical manufacture is vital in minimizing both the type and the number of microorganisms.

Monitoring, in the form of regular surveillance, should include an examination of the microbiological attributes of Pharmacopeial articles and a determination of compliance with such microbiological standards as are set forth in the individual monographs. It may be necessary also to monitor the early and intermediate stages of production, with emphasis being placed on raw materials, especially those of animal or botanical origin, or from natural mineral sources, which may harbor harmful microorganisms not destroyed during subsequent processing. It is essential that perishable components be stored under conditions designed to deter microbial proliferation.

The nature and frequency of testing vary according to the product. Monographs for some articles require freedom from one or more species of selected indicator microorganisms such as *Salmonella* species, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. For some articles, a specific limit on the total aerobic count of viable microorganisms is set forth in the individual monograph. The significance of microorganisms in